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| 10/524,443 | 05/18/2005 | Bertrand Saunier | NIH341.001NP | 4458 |

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KNOBBE, MARTENS, OLSON & BEAR, LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

| EXAMINER | |
|---|---|
| BOESEN, AGNIESZKA | |

| ART UNIT | PAPER NUMBER |
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| 1648 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/524,443 | SAUNIER ET AL. | |
| | Examiner | Art Unit | |
| | Agnieszka Boesen | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-6 and 8-22* is/are pending in the application.

4a) Of the above claim(s) *4,8 and 14-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,6 and 9-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/18/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## TAILED ACTION

The Amendment filed June 21, 2007 in response to the Office Action of March 21, 2007 is acknowledged and has been entered. Claim 5 has been amended. Claim 7 has been canceled. Claims 4, 8, and 14-22 are withdrawn. Claims 1-3, 6, and 9-13 are under examination in the present Office action.

### *Information Disclosure Statement*

The information disclosure statement (IDS) submitted on May 18, 2005 has been considered by the Examiner and the initialed copy thereof is attached with the present Office action.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Rejection of claims 1-3 under 35 U.S.C. 102(b) as being anticipated by Baumert et al. (Journal of Virology, May 1998, IDS of 7/3/2006) as evidenced by US Biological Technical Data Sheet and SIGMA Product Information Sheet **is maintained.**

Applicant's arguments have been fully considered but have not been found persuasive. Applicant argues that the cited reference does not teach every element of the claimed invention. Applicant submitted a comparison chart comparing the reference by Baumert 1998, and the limitations in claims 1-3. Applicant does not expressly argue which limitations of the current

claims are not disclosed by Baumert, however it appears that Applicant intends to argue that the limitation of "precipitate with a polyethylene glycol" is not disclosed by the Baumert, because this particular limitation is highlighted in the provided comparison table. It is noted that the argued limitation of "precipitate with a polyethylene glycol" is not recited in claims 1-3. Claim 3 recites, "precipitate by gradient ultracentrifugation". Baumert discloses precipitation by gradient ultracentrifugation and gradient centrifugation (see page 3832, under Electron microscopy and page 3831). Thus Baumert anticipates all claim limitations. Therefore the rejection is maintained.

Rejection of claims 5-7, and 9-13 under 35 U.S.C. 102(b) as being anticipated by Baumert et al. (Journal of Virology, May 1998, IDS of 7/3/2006) as evidenced by US Biological Technical Data Sheet and SIGMA Product Information Sheet **is withdrawn** in view of Applicants amendment and arguments.

*New rejection in view of Applicant's amendment*

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

**Claims 5, 6, and 9-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baumert et al. (Journal of Virology, May 1998, IDS of 7/3/2006) as evidenced by US Biological Technical Data Sheet and SIGMA Product Information Sheet.**

Applicant amended the claims to recite, " (...) wherein the cells are lysed by incubating the cells in a buffer containing digitonin and protease inhibitors and wherein the concentration of digitonin is less than or equal to 0.25%".

Applicant argues that the cited reference does not teach every element of the claimed invention. Applicant submitted a comparison chart comparing the reference by Baumert 1998, and the limitations in claims 5, 6, and 9-13. Applicant highlighted the limitations of hypertonic and hypotonic shock. The limitations of hypertonic and hypotonic shock and the incubation of cells wherein the concentration of digitonin is less than or equal to 0.25% are not expressly disclosed in Baumert.

However, it would have been obvious to the skilled artisan to treat the cells with hypertonic and hypotonic shock and to adjust the concentration of digitonin to less than or equal to 0.25%, absent unexpected results. It is well know in the art that the hypertonic and hypotonic shock are conditions wherein the cells would be subjected to lysis, which is the objective of the subsequent method step presently claimed and which is taught by Baumert.

Thus one would have been motivated to treat the cells with hypertonic and hypotonic shock for the purpose of lysing the cells and to adjust the concentration of digitonin to less than or equal to 0.25%. Adjusting the concentration of digitonin is merely a question of optimization of lysing conditions.

Therefore the claims would have been *prima facie* obvious to the skilled artisan at the time when the invention was made.

Baumert teaches the other claims limitations as reiterated below.

Claims are drawn to a method for isolating infection defective hepatitis C virus like particles from cells infected with a baculovirus encoding HCV structural proteins, one VLP comprises: E 1 and E2-p7, and another VLP comprises E1 and E2 without p7 proteins. The method comprises incubating the cells in hypertonic solution and hypotonic solution, lysing the infected cells, adding polyethylene glycol, fractionating the precipitate by gradient ultracentrifugation, incubating the cells in a buffer containing digitonin and protease inhibitors, and centrifuging the lysate through a cushion comprising a monosaccharide, disaccharide or polysaccharide. The isolated particles are 50 nm in diameter.

The specification discloses [0054] that the hypertonic buffer is for example Hepes plus glycerol, and the hypotonic buffer is for example Hepes. The specification also discloses that it is also possible to use other components or steps to achieve successive treatment in a hypertonic buffer and a hypotonic buffer. For example, sucrose or hypertonic saline solution can be followed by hypotonic shock.

Baumert et al. teach a method for isolating infection defective hepatitis C virus like particles from cells infected with a baculovirus encoding HCV structural proteins (see the entire document). Baumert et al. disclose isolation of two VLP constructs: E1 and E2-p7, and another VLP construct comprising E1 and E2 without p7 proteins, particles are 50 nm in diameter (see Figure 1, Figure 4 and Materials and Methods –Baculovirus constructs and insects cell cultures, and page 3831). The method disclosed by Baumert et al. comprises incubating the cells in hypertonic solution and hypotonic solution, lysing the infected cells, adding polyethylene glycol, fractionating the precipitate by gradient ultracentrifugation, incubating the cells in a buffer containing digitonin and protease inhibitors, and centrifuging the lysate through a cushion

comprising sucrose, which is a disaccharide (see Materials and Methods -Purification of HCV-like particles, and page 3831). It is noted that Baumert et al. does not use the name polyethylene glycol, but NP-40. NP-40 is a brand name for polyethylene glycol (see USBiological Technical Data Sheet, under Synonyms). It is also noted that Baumert et al. does not use the name protease inhibitors but specifically names the inhibitors. Aprotinin and Leupeptin used in Baumert's method are protease inhibitors as evidenced by SIGMA Product Information Sheet. The ultracentrifugation in Baumert's method is performed under exact the same parameters as described in Example 6 of the specification, Beckman SW55 rotor; 40,000rpm, 2h, 4°C). Thus Baumert et al. anticipates the current claims.

***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground of rejections presented in this Office action.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnieszka Boesen whose telephone number is 571-272-8035. The examiner can normally be reached on 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AB

Agnieszka Boesen, Ph.D.

/Stacy B. Chen/ 9-4-07
Primary Examiner, TC1600